REMARKS

Claim 13 is added herein. No new matter is presented.

I. Information Disclosure Statement

According to the Examiner, in the previous Office Action, the two NPL references, i.e., Teruhisa Ohashi and Osamu Ishizuka, on the IDS, filed 03/12/2007, were not considered because the references failed to disclose, at least, an abstract in English.

In the Response filed November 30, 2010, it was pointed out that the International Preliminary Report on Patentability (Chapter I) with a written opinion of the International Searching Authority filed on December 22, 2006, provides a concise explanation of the relevance of the two NPL references, which are in Japanese. However, the Examiner did not find the argument to be persuasive. The Examiner stated that the Information Disclosure Statements, filed March 12, 2007, January 13, 2009 and February 26, 2009, fail to list the aforementioned International Preliminary Report on Patentability, which would have been considered by the Examiner. Instead, however, that Statement, filed March 12, 2007, lists the aforementioned NPL references that were previously not considered. See reason set forth supra. However, pursuant to the MPEP, specifically 37 C.F.R. § 1.98, the Examiner has considered, and submitted herewith, English-language translations of the aforementioned non-English language references.

Applicants do not agree with the Examiner's reason for not considering the Japanese language references crossed off on the PTO/SB/08 form submitted with the IDS filed March 12, 2007. Simply put, the references and a concise statement of the relevance thereof were of record at the time the IDS was filed on March 12, 2007 and should have been considered by the Examiner as such. It is not clear why the Examiner refers to subsequent IDS's submitted after March 12, 2007 as a reason for not considering references listed on the IDS filed on March 12,

2007. Nevertheless, the Examiner has obtained English translations of the references and the references have been considered based on the English language translations obtained by the Examiner and are cited on the PTO 892 Form accompanying the Office Action. Thus, no further action is believed to be required from Applicants regarding this issue.

II. Claim Rejections - 35 USC § 103

Claims 1-3 and 6 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Shimoyama et al (European Patent Application No. EP1358889A1; cited by Applicant), in view of Garvey et al (U.S. Patent Application Publication No. 2002/0143007A1; cited by Applicant).

Applicants traverse the rejection for the reasons of record and additionally in view of the following.

Specifically, there is no motivation for one of ordinary skill in the art to combine the references as suggested by the Examiner with a reasonable expectation of success in achieving the claimed invention, i.e., a method of treating overactive bladder accompanied with neurogenic disorders. Even if the references could be combined it does not appear that the claimed invention would have been achieved.

Shimoyama does not teach any positive evidence of the treatment of overactive bladder accompanied with neurogenic disorders by administering an alpha receptor antagonist. As noted by the Examiner, Shimoyama et al. disclose a method for the therapy of lower urinary tract symptoms comprising administration of an α receptor blocker to a patient, but Shimoyama specifically discloses that "lower urinary tract symptoms" refers to symptoms of urinary disturbance due to a functional obstruction of lower tract of both males and females, *and does*

not include that which is due to disturbance of nerve controlling the lower urinary tract. Paragraph [0015]. Thus, Shimoyama et al. does not fairly teach or suggest treatment of lower urinary tract symptoms due to a disturbance of nerve controlling the lower urinary tract using the method described therein, i.e., administration of an α receptor blocker to a patient.

Garvey et al. fails to remedy the deficiencies of Shimoyama et al.

Even further, Garvey lists numerous compounds as α-adrenergic receptor antagonists including KMD 3213 and terazosin. Shimoyama also raises terazosin as an α1 receptor blocker (see paragraph [0017]). Rivas, D.A., et al (Neurourology and Urodynamics, Vol. 14, 1995, pp. 141-152, a copy of which is submitted herewith) disclose that terazosin, an alpha-1 antagonist, had no effect on the bladder capacity in a spinal cord injury rat model, while oxybutynin increased bladder capacity (see p.145, from line 4 from the bottom to p.146, line 1, and Fig. 4). Since micturition interval (urinary frequency) relates to the bladder capacity, according to Rivas's teaching, one of skill in the art would not have expected an alpha-1 blocker illustrated in the prior arts always would improve urinary frequency associated with spinal cord injury. On the other hand, the compound of the present invention, especially silodosin (KMD3213), prolonged the micturition interval and decreased the frequency of involuntary contraction in filling phase in the rat spinal cord injured model (see Example 1 and Figs, 1 and 2). Thus, such remarkable effects would not have been expected based on the teachings of the prior art that the time of the present invention. Therefore, for at least this reason, the present invention is unobvious over Garvey and Simoyama.

Even further, Garvey et al. disclose, in the Abstract, methods for treating benign prostatic hyperplasia (or hypertrophy), neurodegenerative disorders, urge incontinence or overactive

bladder, wherein the α-adrenergic receptor antagonist is KMD-3213. See also reference claims 37, 38, 52 and 58. although Garvey et al mentions urge incontinence and overactive bladder as conditions that may be treated, there is no example of such treatment and no guidance or suggestion as to which of the many potential combinations of agents suggested might have been considered for the treatment of these particular conditions amongst all of the conditions listed. Garvey et al. indicates that its claimed invention is for new and improved treatments of sexual dysfunctions, paragraph [0008]. The only *in vivo* examples in Garvey et al relate to sexual dysfunction and do not employ a compound or composition within the scope of the present claims. Further, it is noted that BPH is mentioned as a condition which may be treated and there is no indication of whether the treatment of urge incontinence or overactive bladder is related to or not related to BPH. Thus, Garvey et al is not sufficiently enabling for a method of treatment for overactive bladder accompanied with neurogenic disorders as claimed in present claim 1.

Additionally, Garvey et al discloses the use of compositions comprising (1) at least one nitrosated and/or nitrosylated α-adrenergic receptor antagonist; (2) an α-adrenergic receptor antagonist optionally substituted with at least one NO and/or NO_2 group, and at least one compound that donates, transfers or releases nitric oxide, or elevates levels of endogenous EDRF or nitric oxide, or is a substrate for nitric oxide synthase; or (3) an α-adrenergic receptor antagonist optionally substituted with at least one NO and/or NO_2 group and at least one vasoactive agent and optionally at least one compound that donates, transfers or releases nitric oxide, or elevates levels of endogenous EDRF or nitric oxide, or is a substrate for nitric oxide synthase. See paragraph [0242]. Garvey et al further describes KMD-3213 as an α-adrenergic receptor antagonist (see paragraph [0124]).

Thus, Garvey et al. relates to a composition and method for use comprising administering at least one nitrosated and/or nitrosylated α-adrenergic receptor antagonist along with optional therapeutic agents. Thus, the composition and method of Garvey are different from Shimoyama et al. and from the claimed invention and one of ordinary skill in the art would not have been motivated to modify or combine the teachings of Shimoyama et al. and Garvey et al. to arrive at the claimed invention.

Specifically, Shimoyama et al. does not teach any positive evidence of the treatment of the treatment of overactive bladder accompanied with neurogenic disorders by administering an α- receptor antagonist and Garvey et al. teaches a totally different therapeutic agent, i.e., a composition composed of at least one nitrosated and/or nitrosylated α-adrenergic receptor antagonist. For example, in order to practice the invention of Garvey et al. using KMD-3213, KMD-3213 would either have to be (1) nitrosated or nitrosylated; and/or (2) used in combination with (a) at least one compound that donates, transfers or releases nitric oxide, or elevates levels of endogenous EDRF or nitric oxide, or is a substrate for nitric oxide synthase or (b) at least one vasoactive agent. Thus, the compositions administered by of Garvey et al are different from that employed in Shimoyama et al. and the compounds of formula (I) employed in the method recited in the present claims.

Moreover, Garvey et al. relates to a totally different therapeutic agent and one of ordinary skill would not have arrived at the claimed invention employing a compound of formula (I) for treatment of overactive bladder based on a combination of the cited references. In this regard, Garvey et al. teaches that at least one nitrosated and/or nitrosylated α-adrenergic receptor antagonist is required for the compositions and methods described therein the risk of toxicities

and adverse effects that are associated with high doses of α-adrenergic receptor antagonists can be avoided by the use of nitrosated and/or nitrosylated α-adrenergic receptor antagonists or by the use of at least one α-adrenergic receptor antagonist in combination with at least one nitric oxide donor. Paragraph [0010]. Thus, based on the disclosure of Garvey et al., one of ordinary skill in the art would not have been motivated to employ KMD-3213 which is not nitrosated or nitrosylated and the additional therapeutic agents (a) and (b) above, with a reasonable expectation of success. Even if the references could have been combined, the present invention would not have been achieved.

There is no motivation to combine the references as suggested by the Examiner with a reasonable expectation of success in arriving at the presently claimed invention, particularly since the primary reference does not teach any positive evidence of treatment of overactive bladder accompanied with neurogenic disorders and Garvey et al. is not enabling for treatment of disorders other than those relating to sexual dysfunction. Therefore, Garvey et al. does not remedy the deficiencies of Shimoyama et al. For these additional reasons the present invention is not rendered obvious by the cited references, whether taken alone or in combination.

Accordingly, Applicants respectfully request withdrawal of the rejection.

III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Jennifer M. Hayes/
Jennifer M. Hayes
Registration No. 40,641

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860
WASHINGTON OFFICE
23373
CUSTOMER NUMBER

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